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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/653,294	05/24/1996	CAROL CLAYBERGER	286002020023	5995
25225	7590	07/07/2004	EXAMINER	
MORRISON & FOERSTER LLP 3811 VALLEY CENTRE DRIVE SUITE 500 SAN DIEGO, CA 92130-2332			DIBRINO, MARIANNE NMN	
		ART UNIT	PAPER NUMBER	1644

DATE MAILED: 07/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/653,294	CLAYBERGER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 08 March 2004.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 2-4, 12, 13, 15-21 and 27 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 2-4, 12, 13, 15, 16, 18-21 and 27 is/are rejected.
 7) Claim(s) 17 is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. Applicant's amendment filed 3/8/04 is acknowledged and has been entered.
2. Claims 2-4, 12, 13 and 15-21 and 27 are pending.

Claims 2-4, 12, 13, 15-21 and 27 are presently being examined.

The following grounds of rejection remain.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
4. Claims 2-4, 12, 13, 18-21 and 27 stand rejected under 103(a) as being unpatentable over WO 88/05784 in view of Wong et al (Human Immunology 1992, 35/3, 200-208), U.S. Patent No. 5,073,540 and U.S. Patent No. 5,478,925.

WO 88/05784 teaches peptides which are cross reactive with portions of the $\alpha 1$ or $\alpha 2$ domains of MHC class I, with the sequence of those of the instant claims (especially claim 1 and abstract). WO 88/05784 also teaches modification of such peptides using conventional techniques to extend their biological half lives (especially pages 21-23). Page 10 of the instant application discloses such conventional techniques.

WO 88/05784 explicitly teaches use of such peptides for prolonging graft survival time by reducing rejection caused by CTL. WO 88/05784 teaches using the said peptides linked to other peptides or proteins of interest.

WO 88/05784 does not teach dimerization of the peptides.

Wong et al teaches foci of TCR receptor aggregation upon binding to MHC class I molecules.

Patent No. 5,073,540 discloses peptides useful as antagonists or agonists for membrane receptors, one portion comprising the same structure as the peptides of the instant application (especially columns 7 and 8). Patent No. 5,073,540 further discloses that oligopeptides may be employed that are capable of mimicking the site of the Class I antigen associated with binding to the receptor, thus substituting for the class I antigen (especially paragraph spanning columns 4 and 5).

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U.S. Patent No. 5,478,925 discloses receptors that exist in aggregated form when exposed to ligand. U.S. Patent No. 5,478,925 further discloses binding proteins that are identical to the extra-cellular domains of the said receptors that compete for binding and that the monomers must be administered in very high doses in order to result in effective inhibition of binding when administered to humans. U.S. Patent No. 5,478,925 discloses that multimers of the proteins are more effective in inhibiting activity at lower doses, since they can effectively compete for binding sites on the aggregates of the cell surface receptors. (especially columns 1, 2 and 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the prior art peptides taught by WO 88/05784 as multimers, i.e., at least dimers, as is taught by U.S. Patent No. 5,478,925 for other receptor mimicking and inhibiting polypeptides, and to test functional activity on surface receptors or lymphocyte activity of the modified peptides using the assays taught by WO 88/05784 (especially page 25), and to use the said multimeric peptides in the method of inhibiting graft rejection taught by WO 88/05784 for prolonging graft survival time by reducing rejection caused by CTL which comprise TCR that aggregate upon binding to MHC class I molecules as taught by Wong et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate or inhibit membrane receptors as taught by WO 88/05784 and as disclosed by Patent No. 5,073,540 and/or to prolong graft survival time as taught by WO 88/05784 because Wong et al teaches that TCR on CTL aggregate upon binding class I MHC and U.S. Patent No. 5,478,925 discloses that multimers are more effective in inhibiting activity at lower doses since they can effectively compete for binding sites on the aggregates of cell surface receptors and because one of ordinary skill in the art at the time the invention was made would have expected the dimers of the same unit to exert the same functional effects as a monomer.

Applicant's arguments in Applicant's amendment filed 3/8/04 have been fully considered but are not persuasive.

Applicant's position in the said amendment beginning on page 6 and continuing on to page 10 are of record.

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It is the Examiner's position that U.S. Patent No. 5,478,925 discloses receptors that exist in aggregated form when exposed to ligand, and that multimers of binding proteins that are identical to the extra-cellular domains of the said receptors compete for binding to the ligand of the said receptors, i.e., they are extracellular domains of TNF-Rs, and counteract or downregulate the cytotoxic effects of TNF. The teaching of WO 88/05784 is of peptides that comprise portions of the α 1 and/or α 2 domains of MHC class I that can be used to inhibit CTL-mediated responses including graft rejection, i.e., the soluble class I domain peptides can compete for binding to the CTL (especially page 32 at lines 25-29) and downregulate or counteract the cytotoxic effects of CTL, similarly to the soluble receptors disclosed by U.S. Patent No. 5,478,925. It is the Examiner's further position that although U.S. Patent No. 5,073,540 discloses oligopeptides with the same structure as those of the peptides of the instant application conjugated to another peptide that binds the binding site of a second cell surface receptor (such as a natural ligand or antagonist), U.S. Patent No. 5,073,540 is relied upon for the teaching of the former oligopeptides that mimick the site of the Class I molecule associated with binding to the receptor, thus substituting for the Class I molecule, the same oligopeptides taught by WO 88/05784. Wong is relied upon for the teaching of foci of TCR receptor aggegregation (such as TCR receptors on CTL) upon binding to MHC class I molecules. U.S. Patent No. 5,478,925 is also relied upon for the disclosure that multimers of proteins or peptides are more effective in inhibiting activity at lower doses since they can effectively compete for binding sites on the aggregates of the cell surface receptors and that the TNF-Rs exist in aggregated forms in cells exposed to TNF. With regard to Applicant's arguments as to U.S. Patent No. 5,478,925 (Wallach), that the monomers of Wallach are larger than those of the instant claims, and that Wallach provides no teaching that the multimers of Wallach are useful in any setting other than cytokine-cytokine interactions, the peptide dimers of the instant application "comprise" the SEQ ID NO recited in the instant claims and so do not have length limitation, it is the Examiner's position that the dimers of the instant claims are not length limited as the claims recite "comprising", Wallach is relied upon for the disclosure of an extracellular portion of a receptor TNF-Rs used to block the cytotoxic effects of a molecule to which the receptor binds, that the TNF-Rs exist in aggregated form in cells exposed to their ligand and that multimers of the extracellular portion of TNF-Rs can more effectively compete for binding sites for ligand on aggregates of the TNF-R cell surface receptors, that WO 88/05784 teaches that the soluble class I domain peptides can compete for binding to the CTL potentially through the TCR receptor (especially page 32 at lines 25-29) and downregulate or counteract the cytotoxic effects of CTL, and Wong teaches that TCR receptors aggregate upon binding class I molecules. In addition, it is the Examiner's position that Wong et al teaches in the paragraph spanning columns 1 and 2 on page 206 that previous studies have demonstrated aggregation of Ti/CD3 TCR at the area of contact between the responding T cell and the APC. With regard to Applicant's arguments on pages 8-9 at sections B and C of the said amendment, it is the Examiner's position that the primary reference in the instant rejection to be modified, WO 88/05784, teaches the peptides of the instant claims as a monomer, that WO 88/05784 teaches extending the biological half-lives of

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the said peptides by modifying them and further teaches the use of the said peptides for extending graft survival time by reducing rejection caused by CTL, and that the instant rejection does not propose modification of the fusion peptides of Olsson et al (US Patent No. 5,073,540). It is the Examiner's position that one of ordinary skill in the art at the time the invention was made would have been motivated to multimerize the peptide taught by WO 88/05784 in order to extend it's half-life. With regard to Applicant's argument that use of only a portion of the RNF-R as an inhibitory peptide would improperly change the principle of operation of Wallach's invention, it is the Examiner's position that there is no teaching that truncation of the extracellular portion would abrogate TNF binding. With regard to Applicant's arguments on pages 9-10 at section D of the said amendment, it is the Examiner's position that the combination of references in the instant rejection would predict that dimers of the peptides taught by WO 88/05784 would have superior properties to the monomers in terms of increased half-life and in being more effective in inhibiting CTL activity at lower doses.

5. Claims 2-4, 12, 13, 18-21 and 27 stand rejected under 103(a) as being unpatentable over WO 88/05784 in view of U.S. Patent No. 6,419,931.

WO 88/05784 teaches peptides which are cross reactive with portions of the $\alpha 1$ or $\alpha 2$ domains of MHC class I, with the sequence of those of the instant claims (especially claim 1 and abstract). WO 88/05784 also teaches modification of such peptides using conventional techniques to extend their biological half lives (especially pages 21-23). Page 10 of the instant application discloses such conventional techniques. WO 88/05784 explicitly teaches use of such peptides for prolonging graft survival time by reducing rejection caused by CTL. WO 88/05784 teaches using the said peptides linked to other peptides or proteins of interest when

WO 88/05784 does not teach dimerization of the peptides.

U.S. Patent No. 6,419,931 discloses that peptides that modulate CTL can be combined to form multimers and that the same peptide can be linked to itself to form a homopolymer, i.e., a dimer (especially column 17 at lines 4-38-43).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the prior art peptides taught by WO 88/05784 as dimers as disclosed by taught by U.S. Patent No. 6,419,931, and to test functional activity on surface receptors or lymphocyte activity of the modified peptides using the assays taught by WO 88/05784 (especially page 25), and to use the said multimeric peptides in the method of inhibiting graft rejection taught by WO 88/05784 for prolonging graft survival time.

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One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate or inhibit membrane receptors as taught by WO 88/05784 and to prolong graft survival time as taught by WO 88/05784 because U.S. Patent No. 6,419,931 discloses that peptides that modulate CTL can be combined to form multimers and that the same peptide can be linked to itself to form a homopolymer, i.e., a dimer, and one of ordinary skill in the art at the time the invention was made would have expected the dimers of the same unit to exert at least the same functional effects as a monomer.

Applicant's arguments in Applicant's amendment filed 3/8/04 have been fully considered but are not persuasive.

Applicant's position in the said amendment beginning on page 11 and continuing on to page 12 is of record.

It is the Examiner's position that U.S. Patent No. 6,419,931 discloses that the same peptide can be linked to itself, thereby forming a dimer or homopolymer. U.S. Patent No. 6,419,931 discloses that the CTL express a TCR which is capable of recognizing foreign antigen fragments bound to MHC class I molecules on the surface of APC. It is the Examiner's further position that WO 88/05784 discloses that the subject peptides may be used in combination with antigenic peptides to activate CTLs (page 19), or without combination with antigenic peptides to inhibit CTLs, in either case the class I molecule with or without peptide binds to the TCR. It is the Examiner's position that since U.S. Patent No. 6,419,931 discloses a dimer of a stimulating peptide and WO 88/05784 discloses that the subject peptides may be used in combination with antigenic peptides to activate CTLs (page 19), or without combination with antigenic peptides to inhibit CTLs, that it would also be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have dimerized the peptides taught by WO 88/05784. It is the Examiner's further position that "a peptide dimer" that comprises one of the sequences recited in the instant claims need not be a dimer of the said sequence but a dimer of another sequence, but may comprise the recited sequence.

The following are new grounds of rejection.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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7. Claims 2-4, 12, 13, 15, 18-21 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the . . . claimed subject matter", Vas-Cath, Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed peptide dimer/composition thereof that inhibits cytotoxicity and consists of up to 60 amino acid residues and comprises one of the sequences in the instant claims, or which comprises one or more of the sequences recited in the instant claims, or a method recited in the instant claims for extending the period of acceptance by a recipient of a transplant from an allogeneic or xenogeneic MHC donor comprising administering the said peptide dimer/composition thereof.

The instant claims encompass a peptide dimer/composition thereof comprising up to 60 amino acid residues or of unlimited length, the said peptide dimer comprising one of the 10-mer, 12-mer or 20-mer sequences recited in the instant claims, and capable of inhibiting any type of cytotoxicity. The said peptide dimer/composition thereof can comprise amino acid residues that flank the said sequences in the protein of origin, or can be any number of undisclosed and unrelated sequences. There is insufficient disclosure in the specification on peptides of up to 60 amino acid residues or of unlimited length comprising at least one of the sequences recited in the instant claims.

The specification discloses the 10-mer, 12-mer or 20-mer sequences recited in the instant claims. The specification further discloses that "For the most part, the peptides will be based on a 6 amino acid sequence found at positions 79-84 in the HLA-B [α1-domain] sequence, but may include amino acids related to those at HLA-B positions 60-84 [the B2702.60-84 peptide is disclosed in the instant specification], as well as additional irrelevant sequences", that they are CTL immunomodulating compositions and as such must be shown to inhibit CTL-mediated lysis in cytotoxicity assays and/or inhibit anti-CD3-induced proliferation of purified T cells (page 4 at lines 15-24 and page 6 at lines 3-6). The specification does not disclose any peptides comprising the sequences recited in the instant claims wherein the flanking amino acid residues are not from HLA-B positions 60-84, nor does the specification disclose inhibition of cytotoxicity wherein the inhibition is of CTL-mediated lysis.

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In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as a peptide dimer that "comprises" one of the recited sequences or consists of up to 60 amino acid residues" and comprises one of the recited sequences and "inhibits cytotoxicity", is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of containing one of the recited sequences. It does not specifically define the compounds that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than that they comprise one of the recited sequences. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outline [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

There is no disclosure of a genus of peptide dimers comprising of one of the recited sequences that does not consist of a dimer of the said sequence or consisting of up to 60 amino acid residues and comprising one of the recited sequences. One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

8. Claims 2-4, 12, 13, 15, 18-21 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to make and/or use an isolated peptide dimer/composition thereof that inhibits cytotoxicity and consists of up to 60 amino acid residues and comprises one of the sequences in the instant claims, or which comprises one or more of the sequences recited in the instant claims, or to use the method recited in the instant claims for extending the period of acceptance by a recipient of a transplant form an allogenic or xenogeneic MHC donor comprising administering the said peptide dimer/composition thereof.

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The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a peptide dimer/composition thereof comprising up to 60 amino acid residues or of unlimited length, the said peptide dimer comprising one of the 10-mer, 12-mer or 20-mer sequences recited in the instant claims, and capable of inhibiting any type of cytotoxicity. The said peptide dimer/composition thereof can comprise amino acid residues that flank the said sequences in the protein of origin, or can be any number of undisclosed and unrelated sequences.

The specification discloses the 10-mer, 12-mer or 20-mer sequences recited in the instant claims. The specification further discloses that "For the most part, the peptides will be based on a 6 amino acid sequence found at positions 79-84 in the HLA-B [α 1-domain] sequence, but may include amino acids related to those at HLA-B positions 60-84 [the B2702.60-84 peptide is disclosed in the instant specification], as well as additional irrelevant sequences", that they are CTL immunomodulating compositions and as such must be shown to inhibit CTL-mediated lysis in cytotoxicity assays and/or inhibit anti-CD3-induced proliferation of purified T cells (page 4 at lines 15-24 and page 6 at lines 3-6). The specification does not disclose any peptides comprising the sequences recited in the instant claims wherein the flanking amino acid residues are not from HLA-B positions 60-84, nor does the specification disclose inhibition of cytotoxicity wherein the inhibition is of CTL-mediated lysis.

An undue amount of experimentation would be involved in determining longer peptides from the many possibilities that would be capable of inhibiting any type of cytotoxicity, including CTL-induced cytotoxicity.

Evidentiary reference WO 88/05784 teaches peptides having α 1 or α 2 domains of MHC class I are used for prolonging graft survival time by reducing rejection caused by CTL.

There is insufficient guidance in the specification as to how to make and/or use the instant invention. There is no disclosure in the specification as to which peptide dimers comprising the sequences recited in the instant claims would inhibit cytotoxicity, except for the peptide dimers consisting of the sequences recited in the instant claims. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

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9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 2-4, 12, 13, 16, 20, 21 and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U. S. Patent No. 6,436,903 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application discloses using the claimed peptides together with a subtherapeutic dosage of an immunosuppressant for inhibition of transplantation rejection, and the claims of U. S. Patent No. 6,436,903 B1 encompass a peptide comprising the sequence RENLRIALRY, as do the instant claims.

11. Claims 2-4, 18-21 and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U. S. Patent No. 5,723,128. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application discloses using the claimed peptides together with a subtherapeutic dosage of an immunosuppressant for inhibition of transplantation rejection, and the claims of U. S. Patent No. 5,723,128 encompass a peptide comprising the sequence RENLRIALRY and a method for extending the period of acceptance of an allograft or for blocking CTL activity, as do the instant claims, and the instant specification teaches substitution of amino acid residues, i.e., "mutated".

12. Claim 17 is objected to for depending upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

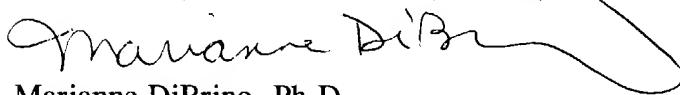
13. It is requested that Applicant correct the spelling of "allogenic" to allogeneic in claim 18.

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14. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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